REMARKS

Claims 1-4, 6, 14-16, and 29 are currently pending. Claims 8, 10-13, 17-28 are withdrawn and 5, 7, 9, and 30 are cancelled.

Claim 1 was amended to delete the previous exclusion of 7 -benzoyl-3-methyl-2(1H)-quinoxalinone and the definition of R^2 has been amended to remove joining R^2 with R^3 to form =O in view of Ali.

Written Description Rejection

Claims 1-3, 6, 14-15, and 29-30 were rejected under 35 USC §112, first paragraph, as containing subject matter that was not described in the specification in such a way to convey that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action at pages 2-3.) In particular, the Patent Office took the position that the exclusion of 7 -benzoyl-3-methyl-2(1H)-quinoxalinone was considered new matter.

At the outset, the instant rejection is moot as to claim 30 because claim 30 has been cancelled. It is therefore requested that the instant rejection be withdrawn as to claim 30.

The exclusion of 7 -benzoyl-3-methyl-2(1H)-quinoxalinone has been deleted from claim 1. In view of this amendment it is believed that the instant rejection has been overcome and withdrawal thereof is respectfully requested.

Obviousness Rejection

Claims 1-4, 6, 14-16, and 29-30 were rejected under 35 USC §103(a) as being unpatentable over US Pat. No. 5,028,606 (the "'606 Patent") in view of US Pat. No. 6,583,144 (the "'144 Patent").

For the reasons set forth below the rejection, respectfully is traversed.

The "606 Patent disclosure set forth in the previous paper submitted by the applicants is incorporated herein by reference. In addition, the compounds of the '606 Patent were found to have the following properties

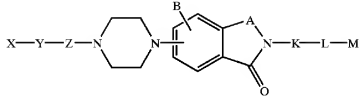
imidazole moiety and by their favourable pharmaceutical properties. In particular the compounds of the invention suppress the plasma elimination of retinoic acids. Further it was found that some compounds of the invention inhibit the formation of androgens from progestines and/or inhibit the action of the enzyme complex aromatase which catalyses the formation of estrogens from androgenic steroids in mammals.

('606 Patent at col. 1.)

The '144 Patent discloses

Disclosed are compounds represented by formula (I) and pharmaceutically acceptable salts and solvates thereof. The compounds can inhibit the biosynthesis of triglycerides in the liver and can inhibit the secretion of lipoprotein containing apolipoprotein B from the liver. Therefore, they are useful for the prevention or treatment of hyperlipidemia (particularly hyper-very-low-density-lipoproteinemia) and arteriosclerotic diseases, such as cardiac infarction, or pancreatitis induced by hyperlipidemia.

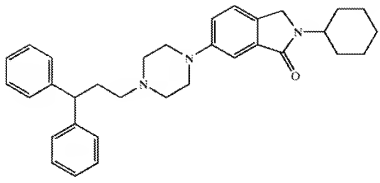
(I)



wherein A represents group $—CR^1R^2—(CH_2)_t—$ where R^1 and R^2 each represent a hydrogen atom or alkyl, —CH═CH—, —O—CH_2—, or —S(O)$_l$—CH_2—; B represents a hydrogen or halogen atom; X represents $—CR^3R^4R^5$, $—NR^6R^7$, $—(CH_2—CH═C(CH_3)—CH_2)_p—$ $CH_2CH═C(CH_3)_2$, alkyl, cycloalkyl, phenyl, cinnamyl, or heteroaromatic ring; Y represents $—(CH_2)_q—$, —CH═CH—, $—NR^8—$, an oxygen atom, or a bond; Z represents carbonyl or a bond; K represents alkylene or a bond; L represents —CH═CH— or a bond; and M represents a hydrogen atom, alkyl, cycloalkyl, phenyl, heterocyclic ring, biphenyl, or diphenylmethyl.

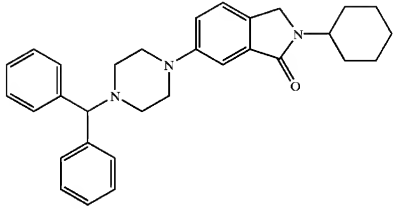
('144 Patent abstract)

Example 8



('144 Patent at col. 69, Ex. 8).

Example 14



('144 Patent at col 71, Ex. 14).

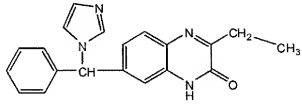
The compounds of the '144 Patent were for found to have the following properties

> The present inventors have now found that novel nitrogen-containing heterocyclic compounds having piperazine on a benzene ring of isoindolone and isoquinolone skeletons or skeletons similar thereto have high activity to reduce the level of lipid in blood, particularly high activity to reduce the level of triglycerides in blood and high activity to reduce the level of lipoprotein containing apolipoprotein B in blood by virtue of inhibitory activity against the biosynthesis of triglycerides and inhibitory activity against the secretion of lipoprotein containing apolipoprotein B in the liver, and thus are useful as therapeutic and prophylactic agents for hyperlipidemia, arteriosclerotic diseases, and pancreatitis.

("144 Patent at col.2).

In making the rejection, the Patent Office asserted that

> US 5,028,606 teaches substituted quinoxalinone derivatives (abstract and Table 9) and disclose the following compound (Table 9, compound 115):



> The reference also teaches a pharmaceutical composition of substituted quinoxalinone derivatives with a pharmaceutically acceptable carrier (column 20, lines 47-58).

(Office Action at pages 4-5.)

The Patent Office acknowledged, however, that the '606 Patent differs from the presently claimed invention

> The difference between the instant compound (compound 1) and that of the prior art is that the instant compound has ethyl groups instead of methyl groups in the position 7 of quinoxalinone ring.

(Office Action at page 5.)

To fill the acknowledged gap, the Patent Office relied upon the '144 Patent as teaching two compounds with and without the addition of CH_2 retain the same biological activity. (*Id.* at 6).

The Patent Office then concluded that

> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the compound taught by US 5,028,066 to arrive at the claimed compound in the field of medicinal chemistry as evidenced by US 6,583,144. In addition, a prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). Notably, the only difference between the prior art and the claimed compound is the addition of a single CH_2 group to the prior art Compound 115 taught by US 5,028,606. However, as noted above, compounds differing by the addition of one CH_2 group are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. Accordingly, in view of *In re Payne* and US 6,583,144, the skilled artisan would have been motivated to make the claimed compound in order to make a similar compound with the expectation that it would have similar properties to that taught by the prior art with a reasonable expectation of success.

With all due respect, it is the claim as a whole that must be considered in making the instant rejection.

> "From the standpoint of patent law, a compound and all of its properties are inseparable; they are one and the same

> thing. The graphic formulae, and the chemical nomenclature, the systems of classification and study such as the concepts of homology, isomerism, etc., are mere symbols by which compounds can be identified, classified, and compared. But a formula is not a compound and while it may serve in a claim to *identify* what is being patented, as the metes and bounds of a deed identify a plot of land, the thing that is patented is not the formula but the compound identified by it."

Regents of University of New Mexico v. Knight, 321 F.3d 1111, 1122 (Fed.Cir. 2003)(Lourie, J.) (quoting *In re Papesch,* 315 F.2d 381, 391 (CCPA1963))(emphasis added).

The Patent Office should make explicit findings on the similarities and differences between the closet prior art species or subgenus of record and the claimed species or subgenus *including findings relating to* similarity of structure, *chemical properties and utilities.*(emphasis added) (MPEP 2144.08 II. A. 2 (8th ed. Rev. 6.)) It is submitted that the Patent Office failed to consider the claim as a whole to the instant facts. In fact, the Patent Office attempted to avoid the required analysis of the differences between the properties by relying on the conclusion that "compounds differing by the addition of one CH_2 group are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties." (Office Action at page 6). However, "the gain or loss of even one methyl group can destabilize the structure." MPEP 2144.08 II.A.4.(c) (8th ed. Rev. 6.))

One of ordinary skill cannot just transpose observations for one chemical series to another totally different chemical series in the hope that it will give the same results. It all depends on the function that the particular group has in the particular compound. It is submitted that the instant facts do not provide a simple routine replacement of a methyl by ethyl as posited by the Patent Office. The position in the core structure that is the focus of the instant analysis concerns a linker between the quinoxalinone ring and the phenyl ring. It is submitted that the '606 Patent does not teach or suggest any degree of freedom for this modification as the Z substituent of the '606 Patent is always directly bond to the carbon atom carrying the imidazolyl. There is no disclosure or suggestion in the '606 Patent that an extra carbon atom may be inserted between the imidazolyl

carrying carbon atom and the quinoxalinone moiety. Such a change would likely alter three dimensional shape of the compound.

The Patent Office relied on the '144 Patent for disclosing modifying a linker from methyl to ethyl of a core structure. Such reliance in misplaced when the compounds being relied on are completely different chemically from the instantly claimed compounds and the '606 Patent compound. The linker in the '144 patent is attached to a pyrazine ring on one end. There is no pyrazine ring in the instant compounds nor is there a pyrazine in the '606 Patent compound relied on the Patent Office. The success of a modification to the core structure depends on the function that the particular group has in the particular compound. Based on the disclosure of '144 Patent it seems that the elongation of the alkyl chain linker does not have an influence on the reported activity, but from this no conclusion, with a reasonable expectation of success, can be drawn for the present compounds or the '606 Patent compounds since these compounds are from a totally different chemical class. Thus, one cannot just predict that the reported modification in '144 Patent will also apply to the compounds of '606 Patent and the present ones.

Moreover, the compounds of '144 Patent are reported as compounds inhibiting the biosynthesis of triglycerides which is clearly different from the activity of '606 Patent compounds which are disclosed as suppressing the plasma elimination of retinoic acid. So a modification that seems to retain activity on biosynthesis of triglycerides does not straightforwardly teach that if the same modification is introduced in compounds suppressing the plasma elimination of retinoic acid (the '606 Patent compound) that these modified compounds would also retain their activity. It depends on what part of the compound is important for activity on the claimed target; it depends on what part of the molecule is essential for binding to its target. It is not seen how one of ordinary skill in the art would increase the length of the linker of the '606 Patent where there is no disclosure about the desirability of doing so nor any suggestion that such a modification would or could result in a compound with the same activity. Because the Patent Office failed to take into account the differences in properties in making the instant rejection, the instant rejection is improper and should be withdrawn.

Obviousness-type Double Patenting

Claims 1-4, 6, 14-16, and 29-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at page 7.) The Office Action alleged that claims1-4, 6, 14-16, and 29-30 of the captioned application "are unpatentable over claims 1, 2, and 7 of co-pending US Patent Application No. 10/595,891 in view of the '606 Patent. The Office Action did not indicate that the rejected claims are otherwise allowable.

The rejection as to claim 30 is moot in view of the cancellation of claim 30 and withdrawal of the rejection is respectfully requested.

Upon notification in the Office Action that claims 1-4, 6, 14-16, and 29 are allowable but for this rejection, the substance of this rejection will be addressed.

Finally, the Examiner is invited to call the applicants' undersigned representative if any further action will expedite the prosecution of the application or if the Examiner has any suggestions or questions concerning the application or the present Response. In fact, if the claims of the application are not believed to be in full condition for allowance, for any reason, the applicants respectfully request the constructive assistance and suggestions of the Examiner in drafting one or more acceptable claims pursuant to MPEP § 707.07(j) or in making constructive suggestions pursuant to MPEP § 706.03 so that the application can be placed in allowable condition as soon as possible and without the need for further proceedings.

Accordingly, entry of the claims and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

Respectfully submitted,

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